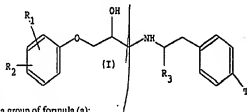
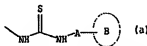


YAMANOUCHI PHARM CO LTD
 96.06.25 96IP-164233 (98.01.13) C07C 335/20, A61K 31/17, 31/24,
 C07D 317/58, A61K 31/275, 31/36
 New thiourea derivatives - are beta-3 receptor agonists which
 accelerate insulin secretion and elevate insulin sensitivity, useful
 for treating diabetes
 C98-041612

Thiourea derivatives of formula (I) and their salts are new.



B(10-A13B, 14-S4) 2



$R_1, R_2 = \text{H, halo, hydroxyl, cyano, nitro, trifluoromethyl, lower alkoxy, lower acylamino, lower alkylsulfonylamino, lower alkoxycarbonylamino, N'-lower alkylureido or lower alkyl (optionally substituted).}$

$R_3 = \text{H or lower alkyl;}$

$A = \text{a bond, lower alkylene or lower alkenylene; and}$
 $\text{ring B} = \text{optionally substituted aryl or cycloalkyl.}$

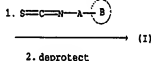
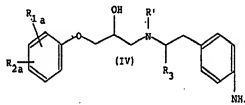
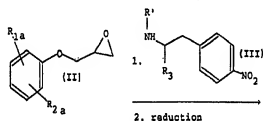
USE

(I) are β -3 receptor agonists and are useful for treating diabetes.
 (I) accelerate insulin secretion and elevate insulin sensitivity.

JP 10007647-A+

PREPARATION

E.g.



$R_{1a}, R_{2a} = \text{protecting group for } R_1, R_2 \text{ and OH; and}$
 $R' = \text{amino protecting group.}$

EXAMPLE

(S)-1-[4-[2-[N-(4-Butoxycarbonyl)-N-(2-hydroxy-3-

JP 10007647-A+/I

98-126135/12

phenoxypyl)amino]ethyl]phenyl]-3-phenylthiourea (0.33 g)
 dissolved in methanol (10 ml) and 4 N hydrogen chloride ethyl acetate
 solution (10 ml) were mixed and stirred at room temperature for 1
 hour to give 0.17 g (S)-1-[4-[2-[(2-hydroxy-3-
 phenoxypyl)amino]ethyl]phenyl]-3-phenylthiourea (Ia).HCl, m.pt.
 214-217 °C. (MHG)
 (20pp0102DwgNo.0/0)

JP 10007647-A/2